Substances Generally Recognized as Safe
Supporting Statement
0910-0342

A. JUSTIFICATION

1. Circumstances Necessitating Information Collection

Section 701 of the Federal Food, Drug, and Cosmetic Act (the act) (21 U.S.C. 348) sets forth authority to issue regulations for the efficient enforcement of the act (Attachment 1).

Section 201 of the act defines terms utilized within the act (Attachment 2). Food is defined by the act (21 U.S.C. 321(f)) to mean A(1) articles used for food or drink for man or other animals, (2) chewing gum, and (3) articles used for components of any such article.@ Thus, the act clearly incorporates animal feed and drink into its definition of food.

Section 409 of the act (Attachment 3) establishes a premarket approval requirement for "food additives." Under section 409 of the act, a producer must demonstrate the safety of a new additive (such as a preservative, antioxidant or emulsifier) to FDA before it can be used in food processing. However, in enacting section 409 of the act, Congress recognized that many substances intentionally added to food do not require formal premarket review by FDA to assure their safety. Congress thus adopted, in section 201(s) of the act (21 U.S.C. 321(s)), a two-step definition of "food additive." The first step broadly includes any substance the intended use of which results or may reasonably be expected to result, directly or indirectly, in its becoming a component or otherwise affecting the characteristics of food, which under section 201(f) includes animal food. The second step, however, excludes from the definition of food additive substances that are generally recognized as safe (GRAS) by qualified experts. It is on the basis of the GRAS exemption to the "food additive" definition that many ingredients are lawfully marketed today without a food additive regulation.

Congress' approach to defining food additive means, however, that a company developing a new food substance (i.e., a substance that will be added directly to food or that will indirectly migrate to food because it is a component of a food-contact article), a new version of an established food substance, or a new process for producing a food substance must make a judgment about whether the resulting substance is a food additive requiring premarket approval by FDA. Under section 409 of the act, manufacturers can determine that use of a food substance is exempt from the statutory premarket approval requirements because it is GRAS and may market such substances without requesting agency concurrence with their determination. However, when a use of substance does not qualify for the GRAS exemption or other exemptions provided under section 201(s) of the act, that use of the substance is a food additive use subject

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to the premarket approval mandated by the act. In such circumstances, the agency can take enforcement action to stop distribution of the food substance and foods containing it on the grounds that such foods are or contain an unlawful food additive.

In 1959-1961, FDA clarified the regulatory status of a multitude of ingredients that were used in food prior to 1958 by amending its regulations to include a list (now 21 CFR parts 182 and 582) of food ingredients whose conditions of use are GRAS. However, many substances that were considered GRAS by the food and feed industry were not included in the agency GRAS list. In 1972, FDA established a voluntary process (21 CFR 170.35(c) and 570.35(c)) whereby manufacturers could petition FDA to affirm that a use of a substance is GRAS. The current voluntary petition process requires that FDA initiate rulemaking by announcing that the agency has filed a petition proposing that a use of a substance is GRAS, conduct a comprehensive review of the submitted data and information and promulgate a regulation affirming that the petitioned use of the substance is GRAS. In practice, FDA has taken years to bring the voluntary petition process to closure and publish a final rule that describes the basis for the agency□s conclusion; manufacturers who submit a GRAS petition frequently market that substance while the petition is under review.

FDA is proposing to eliminate the current voluntary GRAS affirmation petition process and to replace it with a voluntary GRAS notification procedure that would allow FDA to direct its resources to questions about GRAS status that are a priority with respect to public health protection rather than to scrutinizing data and issuing rules. Under the proposal, manufacturers would notify FDA about a claim that a particular use (or uses) of a substance is exempt from the statutory premarket approval requirements based on their determination that such use is GRAS. The notice would include a detailed summary of the basis for the manufacturer□s determination of GRAS status. FDA would, within a period of ninety days, respond to the notifier in writing and could advise the notifier that the agency has identified a problem with the notice.

FDA is proposing procedural regulations (proposed 21 CFR 170.36 (□ 170.36) and 21 CFR 570.36 (□ 570.36) ; attached) that would provide a standard format for the voluntary submission of a notice. FDA would not, however, establish a regulation listing the individual substances that the agency is notified about under proposed □ 170.36 or □ 570.36.

This is a request for OMB approval of the information collection requirements in the proposed regulation □Notice of a Claim for Exemption based on a GRAS Determination.□ The requirement, if the proposed rule becomes final, would be:

21 CFR 170.36 and 21 CFR 570.36

Reporting - specifies the content of a notice that provides the basis for a GRAS exemption claim

Recordkeeping - specifies that the information that provides the basis for a GRAS

exemption claim must be available for FDA review and copying or be sent to FDA upon request

2. How, by whom, and for what purpose information used

Under the proposed notification procedure, FDA does not intend to routinely conduct its own detailed safety evaluation or to affirm that a substance is GRAS for its intended use. Rather, the agency intends to evaluate whether the notice provides a sufficient basis for a GRAS determination and whether information in the notice or otherwise available to FDA raises issues of public health significance that lead the agency to question whether use of the substance is GRAS. Within 90 days of receipt of the notice, FDA would respond to the notifier in writing and could advise the notifier that the agency has identified a problem with the notice.

FDA believes that there will be considerable interest, from a broad segment of the public, including members of the regulated industry, other federal, state, and local government agencies, international government agencies, and public interest groups, in notices received under the proposed regulations. Therefore, FDA is proposing to make readily accessible to the public the information in the notice that describes the GRAS exemption claim and the agency's response to the notice. The entire GRAS notice would be publicly available consistent with the Freedom of Information Act and other federal disclosure statutes.

FDA intends to maintain an inventory of GRAS notices and the agency's response to such notices. Such an inventory would be an administratively efficient mechanism of accounting for the information residing in the publicly accessible file. Such an inventory also would complement the current agency regulations tabulating substances that are listed (21 CFR Parts 182 and 582) or affirmed (21 CFR Parts 184, 186, and 584) as GRAS. FDA intends that such an inventory would also be readily accessible to the public.

3. Consideration of Information Technology

The information in the notice will be narrative text that the agency would read rather than data that the agency would either analyze or store in a database format. FDA would print and copy any notice submitted electronically. Therefore, for efficient enforcement of the act, FDA is requiring the submission of paper copies of the notice. However, FDA is aware that there is an increasing interest in submitting an electronic copy of information prepared for regulatory purposes. Therefore, in the proposed rule FDA is requesting comment on whether it would be appropriate to require or recommend that the submission include an electronic copy, in addition to the three paper copies required under the proposed regulation, of the information in the notice. FDA also is specifically requesting comment on the more narrow question of whether it would be appropriate to require or recommend that the notifier include an electronic copy of the notice□s □GRAS exemption claim,□ which would include succinct descriptions of the notified

substance and applicable conditions of use, to maximize the agency□s flexibility in making such claims publicly accessible .

4. Identification of duplication and similar information already available

Under the Meat and Poultry Inspection Acts, the United States Department of Agriculture□s Food Safety and Inspection Service (USDA/FSIS) has regulatory authority for meat and poultry. Recently, USDA/FSIS (60 FR 67459; December 29, 1995) and FDA (60 FR 67490; December 29, 1995) proposed to amend their regulations to harmonize and improve the efficiency of the procedures used by USDA/FSIS and FDA with respect to reviewing and approving the use of substances in meat and poultry. In the USDA/FSIS proposal, that agency also proposed to adopt the position that substances that are listed in 21 CFR parts 182 or 184 as GRAS for use in food generally, with no limitation other than current good manufacturing practice, would be accepted by USDA as GRAS for use in meat, meat food products, and poultry products generally, unless otherwise restricted for such use by regulation in 9 CFR. Under that proposal, USDA/FSIS would evaluate the suitability of other GRAS substances currently permitted for general food use as to their suitability for specified uses in meat food products and poultry products on a case-by-case basis, in consultation with FDA as appropriate.

Under the proposal to replace the current voluntary GRAS petition process with a voluntary GRAS notification procedure, FDA□s regulations would explicitly state that the act permits the marketing of a GRAS substance without prior approval from FDA and that any person who determines that a particular use (or uses) of a substance is exempt from the statutory premarket approval requirements on the basis that such use is GRAS is responsible for establishing that the determination meets the statutory requirements for exemption, regardless of whether FDA is notified about the determination. FDA interprets the □general recognition□ standard to mean that the information that forms the basis for the GRAS determination must be widely available and ordinarily is published. FDA is proposing that notifiers who voluntarily notify FDA of their GRAS determination summarize, rather than copy and submit, this widely available information to show its relevance to their GRAS determination. Submission of a bibliography or copies of published articles contained in a bibliography, without an analysis of the relevance of the cited literature, is inadequate as a basis for a GRAS determination because it would require FDA, rather than the notifier, to evaluate the information. Such FDA review is inconsistent with one of the objectives of the proposed procedure - i.e., to direct the agency□s resources to questions about GRAS status that are a priority with respect to public health protection rather than to scrutinizing data and issuing rules.

5. Small business

Many firms, large and small, market food substances on the basis of an independent

determination that a use of a substance is GRAS. Most of the GRAS affirmation petitions voluntarily submitted under the existing process, however, are submitted by large chemical manufacturers. FDA believes that the simple format of the notification procedure and rapid agency response conceivably would provide incentive for manufacturers, including small businesses, who independently determine that use of a substance is GRAS to inform FDA of that determination. Thus, FDA expects that the number of notices submitted under the proposed procedure would be greater than the number of petitions submitted under the current process and that a small business is more likely to submit a notice than a petition.

The proposed notification procedure would minimize the burden on all businesses, including small businesses, by providing that the notifier submit a detailed summary of the data and information, rather than the data and information itself, that are the basis for the GRAS determination. The notifier would include a signed statement that the data and information that are the basis for the GRAS determination are available for FDA review and copying at reasonable times or will be sent to FDA upon request. There is no burden to the notifier for developing the data and information that provide the basis for a GRAS determination because such data and information must already be generally available to meet the GRAS standard. Additionally, any person who determines that a substance is GRAS ought to have assembled and evaluated the evidence that forms the basis of such a determination, regardless of whether the person subsequently notifies the agency about the determination. Therefore, the recordkeeping burden on the notifier is the minimal burden of (1) establishing an administrative file that contains the pertinent information and (2) maintaining that file.

6. Consequences of less frequent information collection and technical or legal obstacles

FDA now has more than thirty-five years experience in processing food additive petitions and more than twenty years experience in processing GRAS petitions. As a result of that experience, FDA believes that the petition process, which is the statutorily mandated process for the agency to establish the conditions of safe use for a food additive, should not be applied to GRAS substances, where the conditions of safe use have already been recognized by qualified experts. FDA believes that the lengthy rulemaking associated with the GRAS petition process deters many persons who independently determine that use of a substance is GRAS from informing the agency of such determinations. Moreover, FDA believes that the current commitment of its resources to the GRAS petition process provides limited public health benefit because manufacturers who submit an affirmation petition frequently market the substance of issue before FDA reaches a decision on the GRAS status of its intended use.

Therefore, FDA is proposing to replace the current voluntary GRAS affirmation petition process with a voluntary GRAS notification procedure. FDA has tentatively concluded that the proposed notification procedure has advantages over the current petition process because the resource-intensive rulemaking that is associated with a petition would be eliminated. This

streamlining would allow FDA to redirect its resources to questions about GRAS status that are a priority with respect to public health protection. In addition, the proposed notice is simpler than a GRAS affirmation petition and therefore conceivably would provide an incentive for manufacturers to inform FDA of their GRAS determinations. This would result in increased agency awareness of the composition of the nation□s food supply and the cumulative dietary exposure to GRAS substances. Moreover, FDA has tentatively concluded that the public health would be better served if some resources that are currently directed to the GRAS petition process were redirected to the preparation of documents that would provide the industry with guidance on certain food safety issues for complex substances (e.g., macroingredients or biological polymers, such as proteins, carbohydrates, and fats and oils). Finally, the reduction in resources devoted to the evaluation of GRAS substances would allow FDA to shift resources to its statutorily mandated task of reviewing food and color additive petitions.

A decision by FDA to not replace the current GRAS affirmation petition process with a notification procedure would cause FDA to utilize more resources answering questions about the regulatory status of substances that are not explicitly authorized by the agency□s regulations, particularly for food products offered for import that may be refused entry under section 801 of the act (21 U.S.C. 381) on the grounds that they appear to contain an unapproved food additive. Although FDA does not intend to codify a list of substances that have been the subject of a notice to the agency, FDA does intend to prepare an inventory of such substances, because the agency can most efficiently carry out its responsibilities by having basic information relevant to GRAS exemption claims accessible in a streamlined format.

7. Special circumstances

The proposed notification program, like the current petition process that it would replace, is voluntary. Any person who responds to the agency would do so one time only for any particular use of a substance.

FDA is proposing to require that the notifier retain the information that forms the basis for the GRAS determination and sign a statement that such information is available for FDA review and copying at reasonable times or will be sent to FDA upon request because, under the proposal, notifiers would supply a detailed summary of the information that provides the basis for a GRAS determination rather than the information itself.

8. Outside consultation

The reporting requirement is a proposed rule and has not previously been published in the *Federal Register*. Therefore, although FDA solicited input from representatives of the food industry on the reporting requirements, it could not fully discuss with those representatives the details of the proposed notification procedure. FDA will analyze comments received on the

agency□s estimate of the hourly reporting requirements, and revise that estimate if appropriate, prior to issuing a final rule.

The three members of the industry who were consulted by FDA estimated the hourly burden to prepare a GRAS notice to be 40 to 80, 250, and 100 to 400 hours, respectively. The trade association representative who estimated 250 hours to prepare a GRAS notice stated that the estimate assumed that the preparation of most notices would include review of the manufacturer□s GRAS determination by an expert panel. Such review is common practice in the industry as a means to satisfy the general recognition standard of the statute but is not a requirement under the proposed notification procedure. The manufacturing representative who estimated 100 to 400 hours to prepare a GRAS notice stated that the range of time required was due to the anticipated range of complexity.

9. Payment to respondents

FDA is not proposing any payment or gift to respondents.

10. Confidentiality of information

FDA is proposing that a particular section (i.e., the "GRAS exemption claim") of a notice be immediately available for public disclosure on the date the notice is received. FDA also is proposing that all remaining data and information in a notice will become available for public disclosure, in accordance with 21 CFR part 20, on the date of receipt of the notice. The general recognition standard signifies that neither the proposed use of the substance nor the critical information needed to establish its safety are confidential. Therefore, FDA presumes that a notice will not contain any information that is protected from public disclosure. Moreover, because a GRAS substance may be marketed without prior approval, FDA presumes that, in most cases, submission of a notice will not reflect the notifier's plans about the timing of commercialization, which is arguably confidential commercial information (21 CFR 20.61(b)), because a notifier may market a substance at any time before or after notifying FDA.

FDA is recommending that a notifier who considers that certain information that is contained in the submission should not be available for public disclosure identify as confidential the relevant portions of the submission for FDA consideration. FDA will review the identified information, determine whether that information is exempt from public disclosure under 21 CFR part 20, and release or protect the information in accordance with that determination. In most cases, the agency is likely to determine that all information submitted to support a GRAS determination is available for public disclosure.

11. Sensitive questions

There are no questions of a sensitive nature in a GRAS notice.

12. Burden hours and explanation

FDA estimates the total annual burden for this information collection to be 9,900 hours.

ESTIMATED ANNUAL REPORTING BURDEN					
21 CFR	No. of respondents	Annual Frequency per Response	Total Annual Response	Hours per Response	Total Hours
170.36	50	1	50	150	7500
570.36	10	1	10	150	1500

There are no operating and maintenance costs nor capital costs associated with this collection.

ESTIMATED ANNUAL RECORDKEEPING BURDEN					
21 CFR	No. of record-keepers	Annual Frequency of Recordkeeping	Total Annual Records	Hours per Recordkeeper	Total Hours
170.36(c)(v)	50	1	50	15	750
570.36(c)(v)	10	1	10	15	150

There are no operating and maintenance costs nor capital costs associated with this collection.

During the past ten years, FDA has received, on average, 10 GRAS petitions for human food per year. The number of GRAS petitions received for animal food has been considerably less, approximately 1 submission per year. FDA consulted with one manufacturing firm who estimated that the agency would receive 2-3 times as many notices as petitions. In addition, FDA believes that the simple format of the notification procedure and rapid agency response conceivably would provide incentive for manufacturers who independently determine that use of a substance is GRAS to inform FDA of that determination. FDA therefore is estimating that the

agency would receive approximately 5 times as many GRAS notices as GRAS petitions, or approximately 50 GRAS notices per year for human food. It is anticipated that animal food manufacturers will take increased advantage of the notification procedure due to its simplicity compared to the GRAS petition process. Therefore, the agency expects to receive 10 notices per year for animal food. Each notice must be submitted only once. Therefore, FDA is estimating the total responses per year to be 50 (food) and 10 (feed).

The reporting requirement is a proposed rule that has not previously been published in the *Federal Register*. Although FDA consulted with three members of the food industry to estimate the hourly burden to prepare a GRAS notice, it could not fully discuss with those representatives the details of the proposed notification procedure. Therefore, the estimate may be revised following publication of the proposal.

FDA agrees that there likely will be a range of complexity for notices submitted under proposed □ 170.36 based on differences in the volume of generally available and accepted information about substances that are eligible for the GRAS exemption. For the purpose of estimating an hourly burden to prepare a GRAS notice, FDA is assuming that there will be three categories of complexity - i.e., low, moderate and substantial - and that the percentages of each type of notice will be approximately equal. FDA also is assuming that the two estimates that provided a range of hours did so on the basis of the anticipated range of complexity of a notice and therefore will assume that the low end of the range corresponded to a notice of low complexity, the median of the range would correspond to a notice of moderate complexity and the high end of the range corresponded to a notice of substantial complexity. Finally, FDA is assuming that the estimate that did not provide a range of hours accounted for notices of varying complexity and supplied an average number of hours; for the purpose of this estimate, FDA will consider that estimate as the midpoint in the range of complexity and include that estimated hourly burden in the agency□s estimate of notices of moderate complexity.

Thus, FDA is estimating the hourly burden to prepare a GRAS notice of low complexity as the average of 40 hours and 100 hours, or 70 hours. FDA is estimating the hourly burden to prepare a GRAS notice of moderate complexity as the average of 60 hours, 250 hours, and 250 hours, or approximately 190 hours. FDA is estimating the hourly burden to prepare a GRAS notice of substantial complexity as the average of 80 hours and 400 hours, or 240 hours. Finally, FDA is estimating that the overall average hourly burden to prepare an individual GRAS notice would be the average of the hourly burdens for notices of all complexity, or approximately 165 hours.

13. Annual cost to respondents

There are no costs associated with generating the information because a GRAS determination must be supported by data and information that is generally available and accepted. Thus, this information exists prior to making, or notifying FDA about, a GRAS determination. However,

under the proposal, manufacturers who notify FDA about a GRAS determination must establish and maintain an administrative file that contains the data and information that provides the basis for the GRAS determination. FDA estimates that the one-time process of establishing that file would absorb approximately 10% of the hourly burden already estimated for preparing a GRAS notice (i.e., approximately 15 hours) and that preparation of the submission itself would absorb the remaining 90% of the estimated hourly burden (i.e., approximately 150 hours).

FDA consulted with three members of the food industry to estimate the hourly cost to prepare a GRAS notice and received an estimate of $70 per hour from one of the consulted members. FDA therefore estimates that the cost of submitting a GRAS notice would be the estimated hourly burden (i.e., 165 hours) multiplied by the estimated hourly cost (i.e., $70), or $11,550 per submission. The estimated yearly cost, based on the submission of 50 human food notices per year at a cost of $11,550 each would therefore be $577,500. The predicted cost for 10 animal food notices would be $115,500. Total yearly cost for both human and animal foods is expected to be $693,000. However, the estimate may be revised following publication of the proposal.

14. Annual cost to government

FDA is estimating that the agency will direct approximately 4 full time equivalent positions (FTE□s) to the GRAS notification procedure for human foods. Due to the smaller number of notifications anticipated for animal food, only 1 FTE is expected to be devoted to processing the notices. Based on an average cost of $100,000 per fully supported position, the cost of processing GRAS notifications would be $500,000 per year.

15. Explanation of change in items 13 and 14

The collection of information is a new collection that is the result of a proposal, which is a segment of FDA□s Reinventing Food Regulations part of the President□s National Performance Review, to eliminate the current voluntary GRAS petition process and replace it with a voluntary GRAS notification procedure. The proposed notification procedure would minimize the burden on all businesses, including small businesses, by providing that the notifier submit a detailed summary of the data and information, rather than the data and information itself, that are the basis for the GRAS determination. FDA believes that the substitution of the proposed notification procedure for the current GRAS petition process will not adversely affect the public health because the agency is replacing one voluntary administrative process with a different voluntary administrative procedure that will utilize FDA's resources more effectively and efficiently. FDA believes that the proposed notification procedure has advantages compared to the current GRAS affirmation petition process because the elimination of the resource-intensive rulemaking process as a matter of course for all GRAS petitions, regardless of their public health

significance, would allow FDA to redirect its resources to questions about GRAS status that are a priority with respect to public health protection. In addition, the simple format of the notification procedure and rapid agency response conceivably would provide incentive for manufacturers who independently determine that use of a substance is GRAS to inform FDA of that determination, resulting in an increased agency awareness of the composition of the nation□s food supply and of the cumulative dietary exposure to GRAS substances. Moreover, FDA believes that the public health would be better served if some resources that are currently directed to the GRAS petition process were redirected to the preparation of guidance documents that would assist industry in addressing appropriate food safety issues for novel or complex substances (e.g., macroingredients or biological polymers, such as proteins, carbohydrates, and fats and oils). Finally, the reduction in resources devoted to the GRAS notification procedure relative to the resources devoted to rulemaking for the GRAS petition process would allow FDA to shift some resources to its statutorily mandated mission to review food additive petitions.

16. Statistical reporting

The information obtained from this data collection will not be published.

17. Expiration date on form

There are no reasons why display of the expiration date for OMB approval of the information collection would be appropriate.

18. Exception to Certification Statement

No exceptions to the certification statement identified in item 19 of the instructions for completing OMB Form 83i have been identified.

B. COLLECTIONS OF INFORMATION EMPLOYING STATISTICAL METHODS

This collection of information does not employ statistical methods.